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00:00.000 --> 00:13.900 Support for Yale Cancer Answers comes from AstraZeneca, a biopharmaceutical business that is pushing the boundaries of science to deliver new cancer medicines. More information at [astrazeneca-us.com](http://astrazeneca-us.com).

00:13.900 --> 00:53.900 Welcome to Yale Cancer Answers with doctors Anees Chagpar and Steven Gore. Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week, it is a conversation about myeloproliferative neoplasms with Dr. Nikolai Podoltsev. Dr. Podoltsev is an Associate Professor of Internal Medicine in Hematology and Associate Director of the Hematology/Oncology Fellowship Program at Yale School of Medicine. Dr. Gore is a Professor of Internal Medicine in Hematology and Director of Hematologic Malignancies at Yale Cancer Center.

00:53.900 --> 00:58.100 <vGore>Myeloproliferative, that is such a mouthful.

00:58.100 --> 01:06.200 <vPodoltsev>Well, Steve, this is something I do pretty much every day and this is a group of neoplastic conditions.

01:06.200 --> 01:06.900 <vGore>Well, you mean neoplastic cancer.

01:06.900 --> 01:23.800 <vPodoltsev>Well, it is a cancer. It is a bit different from other cancers though because it may go on for quite some time and sometimes does not even require any intervention. We do call them neoplasms, MPNs not MPDs as we used to, which as you mentioned are diseases.

01:23.800 --> 01:27.700 <vGore>Did I say disease, okay.

01:27.700 --> 01:28.200 <vPodoltsev>You did say diseases, we call them neoplasms, myeloproliferative neoplasms.

01:28.200 --> 01:43.700 <vGore> Which is a fancy way of saying cancer? It seems to me that over the years, hematologists were very phobic about calling these cancers, was that because they did not know they were cancers or they just did not want to upset the patients?

01:43.700 --> 02:01.400 <vPodoltsev>Challenging to say, but in 2005, a major breakthrough happened. This is when we recognized that a lot of these patients have a mutation called JAK2 V617F mutation and it is associated with cancer and I think it became easier for us to call this condition as neoplasms rather than disorders.

02:01.400 --> 02:07.500 <vGore>I see. So, these patients have mutations, that means they are born with them?

02:07.500 --> 02:12.200 <vPodoltsev>No. Most of them if not the overwhelming majority do not have them at birth. They develop during their life.

02:12.200 --> 02:16.500 <vGore> And how does that happen?

02:16.500 --> 02:22.700 <vPodoltsev>It is an influence of outside factors and perhaps some genetic predispositions. These two together can lead to the development of MPNs.

02:22.700 --> 02:31.200 <vGore>I have been watching the HBO Mini Series about Chernobyl and that had a lot of radiation I assume that some of those patients might have gotten some mutations?

02:31.200 --> 02:37.800 <vPodoltsev>Well, I would not be able to speculate about this even though I am looking forward to watching the series myself.

02:37.800 --> 02:41.600 <vGore>So, you do not know whether there was an increase in myeloproliferative neoplasms.

02:41.600 --> 02:50.900 <vPodoltsev>Actually, I cannot say, but I can tell you that for the atomic bomb survivors in Japan, there was increased incidence of chronic myeloid leukemia.

02:50.900 --> 02:51.000 <vGore> Which used to be considered an MPN right?

02:51.000 --> 03:09.900 <vPodoltsev>It is actually MPN. It is myeloproliferative neoplasm, but it is very different from all other ones because now we have a very good targeted therapy for this disease, which is a poster child for targeted therapy, and in fact, patients with chronic myeloid leukemia, they enjoy a life expectancy similar to the general population because of these treatments.

03:09.900 --> 03:12.000 <vGore> I see. So, we are not going to be talking about those tonight.

03:12.000 --> 03:15.600 <vPodoltsev>Up to you. I can still talk about this as well.

03:15.600 --> 03:29.400 <vGore>I think we are going to talk about some of the other ones. So, can we parse that word for our listeners, myeloproliferative and break it down because it so overwhelming to even think about saying that.

03:29.400 --> 03:35.200 <vPodoltsev>Myeloproliferative means increased proliferation of myeloid compartment of the bone marrow.

03:35.200 --> 03:36.700 <vGore> What is myeloid compartment?

03:36.700 --> 03:48.400 <vPodoltsev>So, bone marrow is the factory of all blood cells. And myeloid compartment is responsible for making red blood cells, some of the white cells as well as platelets.

03:48.400 --> 03:48.100 <vGore>That sounds like everything.

03:48.100 --> 03:54.100 <vPodoltsev>Well, there are also lymphoid cells and the myeloid compartment is responsible for those.

03:54.100 --> 04:02.000 <vGore>I see. So, myeloproliferative means that these non-lymphoid things are growing too much.

04:02.000 --> 04:19.700 <vPodoltsev>Correct. So, in fact, if you look at the bone marrow biopsies of those patients, you will find most of them have a lot more than expected of myeloid cells and they spill out in blood. So, most of these patients will have excess of some if not all myeloid elements in blood.

04:19.700 --> 04:26.500 <vGore>How do patients find out that they have one of these myeloproliferative neoplasms?

04:26.500 --> 04:45.400 <vPodoltsev>A lot of times, it is simple CBC, complete blood count, which is performed at the time of their physical. Some of them will present with the most common complication of this condition, which is thrombosis. Arterial thrombosis - strokes and heart attacks, venous thrombosis - pulmonary embolism and clots in the veins in the legs.

04:45.400 --> 04:48.200 <vGore> Well, that sounds really serious.

04:48.200 --> 05:02.100 <vPodoltsev>Correct. And this is actually the major problem with those neoplasms. I think a lot of patients can suffer from this type of complication and even die from them. So, it is important to establish this diagnosis sooner so we can effect those outcomes.

05:02.100 --> 05:04.400 <vGore>But how common are these problems?

05:04.400 --> 05:47.100 <vPodoltsev>So, speaking about the incidence of myeloproliferative neoplasms; we mostly talk about 2 major ones, essential thrombocythemia and polycythemia vera. There is a third common MPN called myelofibrosis. I will put it aside for now and we can talk a little bit more if you want to later on. So from the standpoint of ET and PV, it is about 10 per million per year or something like that, so I think this incidence is not huge, but these patients live for long time and so the number of those patients I am following is accumulating every year because they enjoy a long life expectancy.

05:47.100 --> 05:55.200 <vGore>But when you talk about establishing a diagnosis early, this is not common enough that everyone should be screened right?

05:55.200 --> 06:19.700 <vPodoltsev>I do not think every patient in the primary care setting should be screened for this condition, but a lot of people get complete blood counts done every year and primary care physicians can look at it and will see that there is something present in excess, either red blood cells, hematocrit and hemoglobin may be elevated or platelets may be increased, sometimes there is increase in white cells together with other cell lines.

06:19.700 --> 06:38.400 <vGore>I see. So, I have not really kept up with recommendations for screening in primary care. I remember some years ago, the utility of measuring complete blood counts on an annual basis in asymptomatic patients was questioned, but maybe that has changed. My doctor does it.

06:38.400 --> 06:50.400 <vPodoltsev>My doctor does it as well as you know. So, I am not sure if there are any formal guidelines in that regard, but pretty much everyone who goes to see their primary care physician gets the blood work before or after the visit and that will include CBC.

06:50.400 --> 06:58.500 <vGore>Okay. So, if there is a problem that is clinically apparent, it should show up in a CBC.

06:58.500 --> 07:11.500 <vPodoltsev>Yeah. Some patients will be diagnosed with normal CBC, it does occur. So, for example, some patients present with so-called splenic vein thrombosis, which is thrombosis in the vessels.

07:11.500 --> 07:11.800 <vGore> You just love to use those words.

07:11.800 --> 07:30.400 <vPodoltsev>Thrombosis of the veins in the abdomen and about the third of these patients when tested will have this JAK2 V617F mutation, which I have mentioned before and this may be an indication that they are actually having myeloproliferative neoplasm which went undiagnosed until they presented with a clot.

07:30.400 --> 07:32.900 <vGore> I see. And so, what happens next to such a patient?

07:32.900 --> 08:24.500 <vPodoltsev>So, the main goal of treatment is to prevent first thrombosis or prevent recurrence of thrombotic events. And depending on the condition, polycythemia vera or essential thrombocythemia, patients will receive usually small-dose aspirin as well as cytoreductive therapy for patients who are considered high risk for the development of thrombotic events as well as patients with polycythemia vera who have increased hemoglobin and hematocrit, excess of red blood cells, will have therapeutic phlebotomies similarly to what happens with blood donors, they will be coming to apheresis unit where a unit of blood is taken with the purpose of decreasing their hematocrit to a level of less than 45%, which is considered safe.

08:24.500 --> 08:28.100 <vGore>So, you are actually doing blood letting, like back in the medieval times.

08:28.100 --> 08:37.000 <vPodoltsev>Yeah something like that has been going on for many, many years now and I think probably the oldest treatment we are using still in current practice.

08:37.000 --> 08:39.200 <vGore> But you do not use leeches?

08:39.200 --> 08:40.900 <vPodoltsev>I personally do not.

08:40.900 --> 08:44.700 <vGore>But one could I suppose.

08:44.700 --> 08:56.000 <vPodoltsev>I guess you can, but I think blood letting is more effective.

08:56.000 --> 09:19.100 <vGore>I am sorry, I just had this great image of this old medieval thing with cups and leeches and stuff. But you do not do it that way, you actually use what you would for a blood donation, so just a needle and a bag. Interesting. So, you put them on some anticoagulation, usually aspirin you said.

09:19.100 --> 09:36.800 <vPodoltsev>Yes. If they do not have history of thrombosis and they do not require regular anticoagulation therapy with either Warfarin or direct oral anticoagulants, aspirin 81 mg daily is a good preventive strategy for a lot of patients.

09:36.800 --> 09:48.400 <vGore> Now, you used another big word that I did not understand, cytoreductive, I think cytoreductive, that is 5 syllables. What is that about.

09:48.400 --> 10:04.500 <vPodoltsev>Cytoreduction is reduction of production of blood cells by the bone marrow and it is accomplished by a number of different medications, most of the patients I take care of take medication called hydroxyurea.

10:04.500 --> 10:17.600 <vGore>Hydroxyurea, now as I recall back in the medieval times when I was a medical student that was maybe one of the oldest chemotherapy drugs ever developed, is that the same one?

10:17.600 --> 10:25.200 <vPodoltsev>Yeah. This drug was developed in Germany in 1869. So, it is a 150-year-old drug.

10:25.200 --> 10:30.100 <vGore>1869. Wow! I did not know that we had chemotherapy back then.

10:30.100 --> 11:04.900 <vPodoltsev>I am not sure how it was used between that time and when it was FDA approved in 1967. It was approved for neoplastic disease and interestingly enough, among those was melanoma, resistant chronic myeloid leukemia, recurrent metastatic and inoperable cancer of the ovary. I do not think we are using hydroxyurea for most of them these days, but the most recently approved indication was in sickle cell disease in 1998 to reduce frequency of painful episodes in kids with sickle cell disease.

11:04.900 --> 11:09.200 <vGore> I am fascinated about that history in melanoma and ovarian cancer, but it is probably not germane to talk about that.

11:09.200 --> 11:11.100 <vPodoltsev>Correct. I cannot really say much more about it.

11:11.100 --> 11:31.000 <vGore> Yeah and it would be interesting to know whether there was actually any efficacy for our listening audience, hydroxyurea is usually given as capsules, oral capsules, and at most usual doses, but it sounds like people think of chemotherapy right?

11:31.000 --> 11:48.400 <vPodoltsev>Yeah. Now having said that, it is an antimetabolite and it inhibits DNA synthesis, so it is chemotherapy. We do use it sometimes for patients with acute myeloid leukemia while we are selecting other treatments as a bridge.

11:48.400 --> 11:49.300 <vGore>To knock their counts down?

11:49.300 --> 11:52.200 <vPodoltsev>Correct.

11:52.200 --> 11:52.400 <vGore> And same thing here, you are trying to knock their counts down?

11:52.400 --> 12:05.400 <vPodoltsev>Yes. So, here it is not a temporary treatment usually. These patients who are on hydroxyurea continue to take it for years, trying to control their counts and keep them close to normal or at normal range.

12:05.400 --> 12:09.500 <vGore>And how is that tolerated?

12:09.500 --> 12:26.900 <vPodoltsev>Most of the patients are able to tolerate this treatment, about 20% will be intolerant and the most common side effects are related to skin toxicity, mucosal membrane toxicity, very infrequently patients develop liver function test abnormalities, fever and pneumonitis, inflammation of the lungs.

12:26.900 --> 12:52.300 <vGore>I see. So, overall, usually pretty well tolerated. But you said that most of these patients have a mutation in a specific gene right and you also said that with chronic myeloid leukemia, they had developed some magic bullet drugs because there is a specific gene there, so would it not make sense to develop specific drugs for this JAK2 thing that you were talking about?

12:52.300 --> 13:26.900 <vPodoltsev>We do have a drug which inhibits JAK stat pathway, it is a JAK inhibitor called ruxolitinib, which is available for management of myelofibrosis since 2011, and for second-line treatment of polycythemia if hydroxyurea is not tolerated or is not working, since 2014. Unfortunately, this drug is not as effective as chronic myeloid leukemia medications called tyrosine kinase inhibitors. So, it does not really change the fate of this disease, it does help to control counts similarly to hydroxyurea.

13:26.900 --> 13:33.800 <vGore> Got it. Well, I would like to talk more about that in our second half, but right now we are going to take a short break for a medical minute.

13:33.800 --> 13:52.700 Medical Minute Support for Yale Cancer Answers comes from AstraZeneca, a biopharmaceutical business with a deep-rooted heritage in oncology and a commitment to developing cancer medicines for patients. Learn more information at [astrazeneca-us.com](http://astrazeneca-us.com).

13:52.700 --> 14:30.900 This is a medical minute about colorectal cancer. When detected early, colorectal cancer is easily treated and highly curable. And as a result, it is recommended that men and women over the age of 50 have regular colonoscopies to screen for the disease. Tumor gene analysis has helped improve management of colorectal cancer by identifying the patients most likely to benefit from chemotherapy and newer targeted agents resulting in more patient-specific treatments. More information is available at [YaleCancerCenter.org](http://YaleCancerCenter.org). You are listening to Connecticut Public Radio.

14:30.900 --> 15:05.400 <vGore>Welcome back to Yale Cancer Answers. This is Dr. Steven Gore, and I am joined tonight by my guest Dr. Nikolai Podoltsev,

and we have been discussing myeloproliferative neoplasms, which I am saying faster and faster. So, Nikolai, we were talking about this ruxolitinib drug, which targets the specific gene abnormality and some of these diseases and you sounded kind of disappointed about it, and you said also that it was approved in second line after hydroxyurea, so has anybody actually compared the two, just putting people on hydroxyurea versus putting people on this fancier drug?

15:05.400 --> 15:55.700 <vPodoltsev> They were not compared head to head because the study which looked at ruxolitinib in patients with polycythemia vera did that after patients received hydroxyurea. I have to say that this was compared to the best available therapy and a lot of patients were on hydroxyurea. So, it is not the way to perfectly compare two medications because there was no clear randomization to hydroxyurea, but because most of the patients who were treated with hydroxyurea continued to take it. Ruxolitinib was superior, not only because of that but because it was an effective drug. So, I would say it is nice to have this medication as a second-line treatment for those patients and actually quite a few of my patients are currently taking it because they could not tolerate hydroxyurea.

15:55.700 --> 16:16.700 <vGore>I know that at least the drug company which manufactures that particular drug promotes research or publicizes research from some of their studies, which suggests that with long-term followup, this drug I think improved people's life expectancy right?

16:16.700 --> 16:22.100 <vPodoltsev>This is actually in myelofibrosis.

16:22.100 --> 16:22.200 <vGore>I see. That is another myeloproliferative neoplasm.

16:22.200 --> 16:39.800 <vPodoltsev>Correct. Myelofibrosis is the worst out of three due to significantly diminished life expectancy and we are talking about primary myelofibrosis as well as secondary myelofibrosis, which may develop from polycythemia vera and essential thrombocythemia.

16:39.800 --> 16:45.300 <vGore> And this means scarring tissue in the bone marrow right?

16:45.300 --> 17:14.600 <vPodoltsev>Correct. Scarring in the marrow leads to relocation of marrow stem cells to the spleen and other places in the body as well as multiple other manifestations, which impair quality of life of the patients quite significantly. And for these patients the median life expectancy is about 6 years when compared to polycythemia vera this number is about 14 years and close to 20 years for patients with ET. Those are the patients who are diagnosed after age 60, younger patients have longer life expectancies.

17:14.600--> 17:22.700 <vGore> I see and so it is in the scar tissue, fibrosis thing where the ruxolitinib may be causing people to live longer?

17:22.700 --> 18:10.300 <vPodoltsev>It is not really clear exactly why survival has improved. This is a strong anti inflammatory medication. It helps with

symptoms related to splenic enlargement. It helps with general symptoms those patients suffer from including fatigue, fever, sweats, weight loss, itching. So, some additional analyses of the studies which looked at ruxolitinib for patients with myelofibrosis showed that there may be improvement of survival of about 1.5 years when compared to other treatments. Inflammation is bad for your body, so I guess if you limit it, it may improve this important outcome. But I do not think it is very clear as to why ruxolitinib does that.

18:10.300 --> 18:27.600 <vGore>I see. And I suppose that it would be possible then in the polycythemia vera, that if you follow people long enough and you have compared the hydroxyurea to ruxolitinib if you had long enough, you might see a similar improvement or who knows right?

18:27.600 --> 19:01.700 <vPodoltsev>It is very challenging to study because of very long life expectancy of those patients. So, we spoke about thrombosis as the main complication, both polycythemia vera and essential thrombocythemia may evolve and they may evolve into myelofibrosis as we said, a much worse disease as well as acute myeloid leukemia, another myeloid neoplasm. This particular complication is very feared because it is very challenging to treat patients who develop secondary myeloproliferative neoplasms.

19:01.700 --> 19:07.200 <vGore> And has that been impacted by any of these new drugs?

19:07.200 --> 19:43.300 <vPodoltsev>No. Unfortunately, we do not have disease modifying treatments, which is certainly a significant need for this patient population and this is what they are looking for. So, there is a drug which was most recently approved in Europe, which is from the class of interferons and this is ropeginterferon, which was approved in February of 2019 as a frontline treatment for patients with polycythemia based on the study results conducted in Europe, which showed that it is superior to hydroxyurea in regard to hematological response as well as controlling the number of cells in blood which are positive for JAK2 mutations.

19:43.300 --> 19:51.000 <vGore>I see. But if it is like many other interferon drugs that comes at a cost in terms of symptoms right?

19:51.000 --> 19:56.000 <vPodoltsev>So, it seems that based on the study results, they were equally well tolerated.

19:56.000 --> 19:59.200 <vGore>Really? Most people I have ever treated with interferon have a bad case of flu most of the times.

19:59.200 --> 20:10.700 <vPodoltsev> But this is ropeginterferon. This is the mono-pegylated form and perhaps that changes not only the frequency of its administration but also the side effect profile.

20:10.700 --> 20:10.500 <vGore> I do not know, you are sounding like a drug rep now.



20:10.500 --> 20:15.600 <vPodoltsev> Well, you know, so this drug is not available in the United States and only approved in Europe.

20:15.600 --> 20:25.000 <vGore>I see. So, it is different than the other similarly formulated interferons that used to be used for hepatitis and things like that.

20:25.000 --> 20:37.400 <vPodoltsev>Correct. The drug is similar but different because of the frequency of administration, which is more convenient and less frequent. And also there is now data against hydroxyurea from a European study, which allowed its approval in Europe.

20:37.400 --> 20:42.200 <vGore> I see. So, is it going to be developed or approved here or submitted.

20:42.200 --> 21:09.900 <vPodoltsev>I think there are thoughts about that, but I will not speak for the pharmaceutical company which is developing this drug, I cannot be certain. But one thing I want to mention is that there is no overall survival difference at least as far as we know because you have to follow these patients for a very long time and this is not the short-term endpoint you can look at so quickly after initiation of the study. So, this is based on molecular, so-called molecular responses as well as hematological responses.

21:09.900--> 21:17.000 <vGore> So, in other words, because patients had less circulating cells that have this mutation, that is assumed to be a good thing?

21:17.000 --> 21:33.400 <vPodoltsev>Yeah. We think that if we reduce the circulating clone, that means we can effect disease biology and perhaps prevent its evolution to higher risk disease like myelofibrosis or secondary AML.

21:33.400 --> 21:32.200 <vGore>But we do not really know that right?

21:32.200 --> 21:32.300 <vPodoltsev>Correct.

21:32.300 --> 21:46.300 <vGore>You have gotten some notoriety in the past year by studying that 1867 drug hydroxyurea or whatever it is, like from the Civil War really?

21:46.300 --> 21:52.800 <vPodoltsev>Well, you know, it is interesting that everything new is well forgotten old.

21:52.800 --> 21:53.800 <vGore>It probably sounds better in Russian.

21:53.800 --> 22:13.400 <vPodoltsev>Yes, it is a Russian proverb I have to say. You are correct. So, we investigated the use of hydroxyurea in patients with PV and ET using SEER Medicare database.

22:13.400 --> 22:13.900 <vGore> What does that mean?

22:13.900 --> 22:46.000 <vPodoltsev> All of the patients who have Medicare, they are registered somewhere and there is this data which is accumulated about them including prescriptions they receive for different medications like hydroxyurea and we capitalize on that. I have connected this particular Medicare data set with SEER, which collects data on cancer diagnosis and we were able to

connect patients who have diagnosis of ET and PV to intake of hydroxyurea or at least the number of prescriptions these people received for this medication.

22:46.000 --> 23:06.400 <vGore>So, let me get this straight. This database, which I think is probably maintained by the National Cancer Institute, links this cancer data, which lets you see who has these diseases you are interested in and then it is connected to their Medicare claims to say which drugs they are getting?

23:06.400 --> 23:07.000 <vPodoltsev>That's correct.

23:07.000 --> 23:13.800 <vGore> Okay. So, you could find out which patients with these diseases are taking any drug?

23:13.800 --> 23:49.900 <vPodoltsev>Correct. We were specifically interested in hydroxyurea because current guidelines recommend it as a first-line treatment for patients with high-risk ET and PV, and the definition of high-risk is related to characteristics which were found to be connected with higher incidence of clots, arterial or venous thrombosis. So, our patient population was 66 years of age or older and patients who are older than 60 are already considered high risk because in general this patient population has higher incidence of arterial or venous clots.

23:49.900--> 23:53.700 <vGore> You mean, just because of their age, they are high risk?

23:53.700 --> 24:29.300 <vPodoltsev>Just because of their age right. So, that made our work somewhat simpler. We looked at incidence of thrombosis in those patients as well as their survival. We also looked in polycythemia vera patients, we looked at the therapeutic phlebotomy use and we analyzed this data and discovered that use of phlebotomy and hydroxyurea was associated with better outcomes, specifically in both essential thrombocythemia and polycythemia vera, patients had better survival as well as decreased incidence of thrombotic events.

24:29.300 --> 24:31.400 <vGore>How big was the difference?

24:31.400 --> 24:51.300 <vPodoltsev>The difference was reasonably significant. We appreciated that those who were treated with phlebotomy among polycythemia vera patients got a 35% reduction in death and 48% reduction in the risk of thrombosis.

24:51.300 --> 24:53.500 <vGore> That is a lot.

24:53.500 --> 25:08.800 <vPodoltsev>Yes. And we also looked at the use of hydroxyurea in this group of patients, and every 10% increase in the proportion of days covered by hydroxyurea treatment was associated with 8% lower risk of death and thrombosis.

25:08.800 --> 25:14.600 <vGore>So, for every 10% more that you took the drug, you get 8% less chance of dying?

25:14.600 --> 25:18.500 <vPodoltsev>And thrombotic events right. Yes, both of them 8%.

25:18.500 --> 25:36.200 <vGore>Gotcha. So, if you are 100% more, that would be 10 times that or something. And is it not possible that the doctors who are prescribing one thing or another, patients are different or maybe just the healthier patients are getting the drug?

25:36.200 --> 26:00.600 <vPodoltsev>We tried to adjust for multiple things including comorbidities, including socioeconomic status. Of course this is a retrospective study and as any retrospective study, it may have certain shortcomings. Having said that, we are confident in our data and the fact that hydroxyurea and phlebotomy use is associated with improved outcomes in these patients.

26:00.600 --> 26:04.800 <vGore>Was that surprising? I mean, people have been prescribed this for a long time right?

26:04.800 --> 26:19.400 <vPodoltsev>Yes, but there is concern that hydroxyurea for example is underused because of its stigma as a chemotherapy drug which may predispose to the development of cancer.

26:19.400 --> 26:23.300 <vGore>I see. Do you think there has been reluctance to use it on some practitioner's or patient's parts?

26:23.300 --> 26:48.700 <vPodoltsev>Correct. Also, the European LeukemiaNet guidelines were published in 2011 and NCCM guidelines came up with their version of MPN guidelines in 2017. So, perhaps familiarity over the guidelines is not fully there and further education of providers taking care of these patients may improve this type of drug utilization.

26:48.700 --> 26:55.200 <vGore> I see. So, NCCN is the an American set of guidelines from various cancer centers right?

26:55.200 --> 26:59.500 <vPodoltsev>Correct and Yale Cancer Center is participating in NCCM.

26:59.500--> 27:02.500 <vGore> I see, and this European one, do they both recommend hydroxyurea?

27:02.500 --> 27:15.200 <vPodoltsev>Yes they do. Both of them recommend hydroxyurea as one of the frontline treatments for patients with polycythemia vera and essential thrombocythemia who require cytoreductive therapy.

27:15.200 --> 27:23.600 <vGore>There is that word again. So, is this really one of the first studies to validate this improvement?

27:23.600 --> 28:00.500 <vPodoltsev>For patients we have 2 studies: One of them is for PV and another one is for ET. And for PV, which is P vera, if you are using this abbreviation, which may not be familiar to all of our listeners, for PV, I would say the data behind guidelines recommended cytoreductive therapy with hydroxyurea was quite weak, it is based on old polycythemia vera group studies and some other retrospective analysis. So, I think adding to the bulk

of this data helps to convince some people to use this medication for high-risk patients with polycythemia vera.

28:00.500 --> 28:02.000 <vGore> What kind of feedback have you gotten since the publication of the paper?

28:02.000 --> 28:22.300 <vPodoltsev>In general, what this published paper does, is it supports current guidelines and we see that guidelines are using more and more frequently, you know I cannot say that this is my doing, but I hope that there was some small contribution from me to that as well.

28:22.300 --> 28:52.600 <vGore>I think it is pretty important that when I first heard that you were doing this research, I honestly said really you are going to study hydroxyurea, I mean how boring is that and yet when you look and say that we have a lot of practices and they have never really been tested right and you have really shown something that means pretty impressive survival benefit.

28:52.600 --> 28:57.700 <vPodoltsev>I agree and I think it helps my patients and my discussion with my patients to understand the potential benefit.

28:57.700 --> 29:28.200 Dr. Nikolai Podoltsev is an Associate Professor of Internal Medicine in Hematology and Associate Director of the Hematology/Oncology Fellowship Program at Yale School of Medicine. If you have questions, the address is [canceranswers@yale.edu](mailto:canceranswers@yale.edu) and past editions of the program are available in audio and written form at [YaleCancerCenter.org](http://YaleCancerCenter.org). We hope you will join us next week to learn more about the fight against cancer here on Connecticut Public Radio.